REMARKS

Amendments to the Claims

Claims 1-25 are currently pending. Claims 1, 2, and 8 have been amended. Claims 12 and 16-19 were previously canceled without prejudice or disclaimer. Claims 4-5, 7, 13-15, and 20-25 were previously withdrawn as drawn to a non-elected invention.

Claims 1, 2 and 8 have been amended to recite that the assay systems employ the use of PRKC-iota. Support for the amendments can be found throughout the specification and particularly at pages 4 and 40-42.

The claim amendments are made solely in an effort to advance prosecution and are made without prejudice, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter. No new matter has been added by way of these amendments.

Priority

The claims, as amended, are directed to methods for identifying a candidate beta catenin pathway by detecting a change in the expression of PRKC- iota. The Office indicated that the priority application, USSN 60/495,172, supports the claimed assay system using PRKC-iota. Accordingly, Applicants respectfully submit that the instant claims are entitled to a priority date of August 14, 2003, the filing date of the 60/495,172 application.

Rejection of Claims Under 35 U.S.C. § 102

Claims 1, 2, 6, 8, and 9 stand rejected under 35 U.S.C. 102(b) as allegedly anticipated by Murray et al (J. Biol. Chem., 268:15847-15853 (1993)) ("Murray"). Applicants respectfully traverse the rejections.

The Office alleged that Murray discloses a first system in which cells are contacted with antisense against PKC and assayed for PKC expression (allegedly

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anticipating steps (a)-(d)) and further disclose a second assay system in which cells that express PKC- α, -β_{II}, and -ζ are contacted with antisense against PKC-β_{II} and assayed for proliferative phenotype (allegedly anticipating steps (e) – (h) because measuring changes in cell proliferation is one way of measuring changes in the beta catenin pathway). Thus, the Office concludes that Murray anticipates the instantly claimed methods.

Under 35 U.S.C. § 102, a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987); *Structural Rubber Products Co. v. Park Rubber Co.*, 749 F.2d 707, 716 (Fed. Cir. 1984) (All elements of the claimed invention must be contained in a single prior art disclosure and must be arranged in the prior art disclosure as in the claimed invention); M.P.E.P § 2131. The identical invention must be described or shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); *Chester v. Miller*, 15 USPQ2d 1333 (Fed. Cir.1990); M.P.E.P. § 2131.

Applicants submit that Murray does not teach all of the elements of the presently claimed methods. The claims, as amended, recite a method of identifying a candidate beta catenin pathway modulating agent using a double assay system comprising Protein Kinase C-iota. The studies preformed by Murray are limited to PMA effect on the proliferation of K562 cells. Murray teaches that the PMA-treated K562 cells express PKC- α, -β_{II}, and -ζ isoforms, but not PKC-β_I, - ε, -δ, or -γ isoforms. Murray is silent as to whether K562 cells express PKC-iota. In view of the fact that Murray provides no teaching whatsoever with respect to PKC-iota, it fails to teach the claimed invention which requires, *inter alia*, providing a first assay system capable of detecting Protein Kinase C-iota expression, measuring the expression of PRKC-iota in the presence or absence of a test agent, detecting a change in the expression PRKC-iota in the presence of the test agent and providing a second assay system comprising cultured cells expressing PRKC-iota.

Applicants submit that the Murray do not anticipate the present claims because it fails to teach each and every step of the claimed methods. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 USC § 102 (b).

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Rejection of Claims Under 35 U.S.C. § 103

Claims 1, 2, 6, and 8-10 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over Murray (J. Biol. Chem. 268:15847-15853 (1993)) in view of Summerton et al., (Antisense & Nucleic Acid Drug Dev., 7: 187-195 (1997)) ("Summerton"). Applicants respectfully traverse the rejections.

The Office alleged that Murray discloses a first system in which cells are contacted with antisense against PKC and assayed for PKC expression, but admitted that Murray does not teach the use of a PMO oligonucleotide. However, the Office alleged that Summerton teaches that PMO oligonucleotides overcome the problems associated with first generation antisense chemistries. The Office concluded that one of ordinary skill in the art would have been motivated to substitute PMO oligonuclotides for the standard oligonucleotide chemistry of Murray.

To meet the requirements for a *prima facie* case of obviousness, the Office must demonstrate that the references teach or suggest all the limitations of the claims. Post-KSR, the Board of Patent Appeals and Interferences (BPAI) has continued to maintain that:

> [A]n examiner must make "a searching comparison of the claimed invention — *including all its limitations* - with the teaching of the prior art." *In re Ochiai,* 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis added). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.,* 349 F.3d, 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka,* 490 F.2d 981, 985 (CCPA 1974)). *Ex Parte* Wada, BPAI, Appeal 2007-377, page 7 (Jan. 15, 2008) (unpublished). *See also, Ex parte* Shepard, BPAI, Appeal 2008-0401, page 7 (Jan. 3, 2008)(unpublished).

Applicants submit that Murray and Summerton, alone or in combination, fail to teach or suggest a method for identifying a candidate beta catenin pathway modulating agent using a double assay system that involves, among other things, measuring and detecting a difference in the expression of PRKC- iota in the presence and absence of a

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test agent. First, as discussed above, Murray does not even mention PRKC-iota and therefore provides no teaching whatsoever relating to this gene or its expression, much less its use in a double assay system for identifying a candidate beta catenin pathway modulating agent. Summerton fails to cure the deficiencies of Murray. Summerton is merely a review article directed to morpholino antisense oligomers, which fails to even mention PKC or the beta catenin pathway. In the absence of any teaching whatsoever regarding PRKC-iota, much less its use in a double assay system to identify a candidate beta catenin pathway modulating agent, the combined teachings of Murray and Summerton fail to teach the elements of the claimed invention.

Furthermore, one skilled in the art would not have been motivated to modify the combined teachings of Murray and Summerton to arrive at the presently claimed screening assay methods. First, neither Murray nor Summerton are concerned at all with the beta catenin pathway and thus provide no teaching whatsoever relating to beta catenin or the pursuit of agents that modulate the beta catenin pathway. Furthermore, both Murray are Summerton are completely silent with respect to the PRKC-iota gene and therefore provide no teaching whatsoever relating to this gene, much less a teaching or suggestion to use this gene in an assay to identify beta catenin pathway modulating agents.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness because the cited references, alone or in combination, fail to teach or suggest all of the limitations of the claimed methods. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection based on Murray et al. and Summerton et al.

Claims 1-3, 6, 8, 9, and 11 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over Murray et al. (J. Cell Biol., 145: 699-711 (1999) ("Murray 1") in view of Murray et al. (J. Biol. Chem. 268:15847-15853 (1993)) ("Murray 2"). Applicants respectfully traverse the rejections.

The Office alleged that Murray 1 teaches that overexpression of $PKC\beta_{II}$ induces colonic hyperproliferation and increases sensitivity to colon carcinogenesis in a transgenic mouse model. The Office further alleged that Murray 2 teaches that

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transgenic PKCβ mice exhibit elevated colonic beta catenin, indicating that PKCβ stimulates the Wnt/APC/beta catenin proliferative signaling pathway. The Office stated that Murray 1 does not teach the treatment of cells with antisense PCKβ. The Office alleged that Murray 2 shows that antisense PCKβ can inhibit the proliferation of PMA-withdrawn cells, confirming the role of PCKβ in cellular proliferation. The Office concluded that one of ordinary skill in the art would have been motivated to use the antisense of Murray 2 to treat the colonic cells of the mouse of Murray 1 in order to confirm that the activity of PKCβ in those cells was responsible for the observed phenotype. The Office reasoned that, in so doing, one would have taken the PKCβ antisense (allegedly anticipating claims 1, 2, 6, 8, and 9) and applied it in a second, animal-based model system in which the animal mis-expresses beta catenin, thereby rendering obvious the invention as a whole. Office Action, at page 9.

As discussed previously, to meet the requirements for a *prima facie* case of obviousness, the Office must demonstrate that the references teach or suggest all the limitations of the claims. Applicants submit that teachings of both Murray 1 and Murray 2 are limited to the study of $PKC\beta_{II}$ and provide no teaching whatsoever relating to PRKC-iota. Murray 1 merely teaches a $PKC\beta_{II}$ transgenic mouse that has elevated colonic beta catenin levels. Murray 2 teaches that $PKC\beta_{II}$ antisense can decrease proliferation in PMA-treated human erythroleukemia (K562) cells, which express PKC- α, -β_{II}, and -ζ, but not PKC-β_I, - ε, -δ, or -γ. Neither reference is concerned with the PRKC-iota gene. Nor are either of the references concerned with identifying beta catenin pathway modulating agents. In the absence of any teaching whatsoever regarding PRKC-iota, much less its use in a double assay system to identify a candidate beta catenin pathway modulating agent, the combined teachings of Murray 1 and Murray 2 fail to teach the elements of the claimed invention.

Furthermore, one skilled in the art would not have been motivated to modify the combined teachings of Murray 1 and Murray 2 to arrive at the presently claimed screening assay methods. Both Murray 1 are Murray 2 are completely silent with respect to the PRKC-iota gene and therefore provide no teaching whatsoever relating to this gene, much less an involvement in the beta catenin pathway. Nor would one

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skilled in the art have any reason to believe that PRKC-iota was involved in the beta catenin pathway based on the teachings of Murray 1 and Murray 2. Murray 2 teaches that PKC isoforms are differentially expressed and have different functions in cells. For example, Murray 2 teaches that PKC-α is involved in the differentiation pathway in K526 cells, while PKC-βII is involved in the proliferative pathway. In the absence of any teaching or suggestion relating to PKC-iota and a connection to the beta catenin pathway, one skilled in the art would not have been motivated to use PKC-iota in a screening assay to identify beta catenin modulating agents.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness because the cited references, alone or in combination, fail to teach or suggest all of the limitations of the claimed methods. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection based on Murray 1 and Murray 2.

Conclusion

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the examiner believes a teleconference will advance prosecution, he is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

Dated: September 13, 2010

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